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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/457,926	12/08/1999	BURTON G. CHRISTENSEN	P-061-R2	8221

22852 7590 08/12/2008

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ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
08/12/2008	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte
BURTON G. CHRISTENSEN, EDMUND J. MORAN, JOHN H. GRIFFIN, MATHAI MAMMEN, J. KEVIN JUDICE, JAMES AGGEN, YONGQI MU, and PACE L. JOHN

Appeal 2007-3886[1]
Application 09/457,926
Technology Center 1600

Decided: August 12, 2008

Before DEMETRA J. MILLS, LORA M. GREEN, and FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to antibiotic compounds. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] Heard July 8, 2008.

STATEMENT OF THE CASE

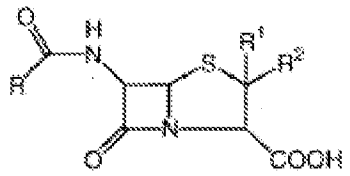
Claims 41-46, 49-51, 53-55, 57, and 58 are pending (*see* App. Br. 3).[2] Claims 42, 44-46, 57 and 58 have been withdrawn from consideration by the Examiner (*id.*). Claims 41, 43, 49-51, and 53-55 stand finally rejected (*id.*). Claim 41 is representative of the appealed subject matter and reads as follows:

41. A compound of the formula:

L'-X'-L"

or a pharmaceutically acceptable salt thereof; wherein
L' is a moiety selected from the group consisting of:

(i) a moiety of formula (a):



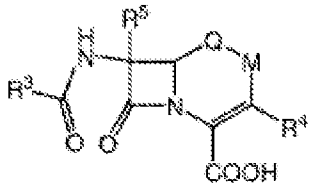
(a)

wherein:

R is selected from the group consisting of substituted alkyl, aryl, aralkyl, and heteroaryl wherein each of said substituents optionally links (a) to the linker via a covalent bond or R is a covalent bond that links (a) to the linker; and

R^1 and R^2 are, independently of each other, alkyl or at least one of R^1 or R^2 is a covalent bond linking (a) to the linker provided that only one of R, R^1 or R^2 links said moiety to said linker;

(ii) a moiety of formula (b):



(b)

wherein:

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[2] Amended Appeal Brief filed January 11, 2007.

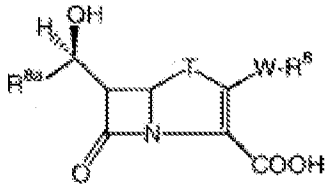
one of M and Q is O, S, or -CH_2- and the other is -CH_2-;

R^3 is selected from the group consisting of substituted alkyl, heteroarylalkyl, aralkyl, heterocyclylalkyl, and -$C(R^6)$=NOR^7, wherein R^6 is aryl, heteroaryl, or substituted alkyl and R^7 is alkyl or substituted alkyl and further wherein each of said substituents optionally links (b) to the linker via a covalent bond or R^3 is a covalent bond that links (b) to the linker; and

R^4 is selected from the group consisting of hydrogen, alkyl, alkenyl, substituted alkenyl, substituted alkyl, halo, heteroarylalkyl, heterocyclylalkyl, -SR^a and -CH_2SR^a, where R^a is aryl, heteroaryl, heterocyclyl or cycloalkyl wherein each of said substituents optionally links (b) to the linker or R^4 is a covalent bond that links (b) to the linker provided that only one of said R^3 substituents or covalent bond and R^4 substituents or covalent bond links said moiety to said linker; and

R^5 is selected from the group consisting of hydrogen, hydroxy; and alkoxy;

(iii) a moiety of formula (c):



(c)

wherein:

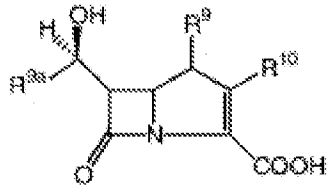
T is S or CH_2,

R^{8a} is alkyl;

W is selected from the group consisting of O, S, -OCH_2-, and CH_2; and

R^8 is -(alkylene)-$NHC(R^b)$=NH where R^b is a covalent bond that links (c) to the linker; or -W-R^8 is a covalent bond that links (c) to the linker provided that only one of R^b or -W-R^8 binds said moiety to said linker;

(iv) a moiety of formula (d):



(d)

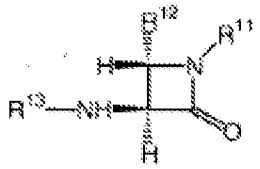
wherein:

R^9 and R^{9a} are alkyl;

R^{10} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, halo, aryl, heteroaryl, heterocyclyl, aralkyl, heteroaralkyl, heterocyclylalkyl and $-CH_2SR^a$, where R^a is aryl, heteroaryl, heterocyclyl or cycloalkyl wherein each of said substituents optionally links (d) to the linker or at least one of R^9 and R^{10} is a covalent bond that links (d) to the linker; or

R^9 and R^{10}, together with the carbon atoms to which they are attached, form an aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, or heterocyclyl ring of from 4 to 7 ring atoms wherein one of the ring atoms optionally links (d) to the linker provided that only one of said substituents, ring atoms, R^9 or R^{10} links said moiety to said linker; and

(v) a moiety of formula (e):



(e)

wherein:

R^{11} is selected from the group consisting of $-SO_3H$ or -(alkylene)-COOH;

R^{12} is selected from the group consisting of alkyl, substituted alkyl, haloalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, substituted cycloalkyl, and heterocyclyl wherein each of said substituents optionally binds (e) to the linker or R^{12} is a covalent bond that links (e) to the linker,

R^{13} is selected from the group consisting of alkyl, acyl, or $-COC(R^{I4})=N-OR^{15}$ wherein R^{14} is aryl or heteroaryl which optionally links (e) to the linker, and R^{15} is -(alkylene)-$COOR^{16}$ wherein R^{16} is hydrogen or a covalent bond that optionally links

(e) to the linker or R^{13} is a covalent bond that links (e) to the linker provided that only one of R^{12}, R^{13}, R^{14} or R^{15} links said moiety to said linker;

L" is an optionally substituted vancomycin moiety or an aglycon derivative of an optionally substituted vancomycin moiety, wherein L" is attached to the linker at a position selected from the group consisting of the carboxy terminus, the amino terminus, the dihydroxyphenyl ring, the saccharide amino group and the aglycone hydroxy terminus; and

X' is a linker of the formula:

$$-X^a-Z^a-(Y^a-Z^a)_m-X^a-$$

wherein

m' is an integer of from 0 to 20;

X^a at each separate occurrence is selected from the group consisting of -O-, -S-, -NR'-, -C(O)-, -C(O)O-, -OC(O)-, C(O)NR'-, -NR'C(O)-, C(S),-C(S)O-, -C(S)NR'-, NR'C(S)-, and a covalent bond;

Z^a at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cycloalkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond;

each Y^a at each separate occurrence is selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR'-, -S(O)n-, -C(O)NR'-, -NR'C(O)-, -NR'C(O)NR'-, NR'C(S)NR'- C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-, $-S(O)_nCR'R"-$, $-S(O)_n-NR'-$, $-NR'-S(O)_n-$, -S-S-, and a covalent bond; where *n* is 0, 1, or 2; and

R' and R" at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic;

provided, that when L" is a vancomycin moiety attached via its carboxyl group to the linker, then L' is not a cefalexin moiety attached to the linker via acylation of its α-amino group.

The Examiner made a species election requirement (*see* Requirement for Restriction/Election 3 (mailed February 20, 2001)). In response, Appellants selected species 2 as the β-lactam moiety at position L' of formula L'-X'-L" in claim 41, vancomycin as the species of glycopeptide antibiotic at position L", and the linkage through the vancosamine nitrogen atom of vancomycin as the moiety X' linking the β-lactam and vancomycin residues (*see* Reply To Requirement for Restriction 3-4 (entered March 19, 2001)).

We limit our consideration of the appealed rejection to the elected subject matter. *See Ex parte Ohsaka*, 2 USPQ2d 1461 (Bd. Pat. App. Int. 1987).

The Examiner applies the following documents in rejecting the claims:

Truett ("Truett I")	US 5,693,791	Dec. 2, 1997
Truett ("Truett II")	US 6,437,119 B1	Aug. 20, 2002

Michael Boeckh et al., "Pharmacokinetics and Serum Bactericidal Activity of Vancomycin Alone and in Combination with Ceftazidime in Healthy Volunteers," 32 *Antimicrob. Agents and Chemotherapy*. 92-95 (Jan. 1988).

M. Renoud-Grappin et al., "Imidazo[1,5-*b*]pyridazine-d4T conjugates: synthesis and anti-human immunodeficiency virus evaluation," 9 *Antiviral Chem. & Chemotherapy* 205-221 (1998).

Thomas Staroske, et al. "Synthesis of Covalent Head-to-Tail Dimers of Vancomycin," 39 *Tetrahedron Letters* 4917-4920 (1998).

The following rejection is before us for review:

Claims 41, 43, 49-51, and 53-55 stand rejected under 35 U.S.C. § 103(a) as obvious over Truett I, Truett II, Boeckh, Renoud-Grappin, and Staroske (Ans. 3-7).[3]

OBVIOUSNESS

ISSUE

The Examiner cites Truett I as teaching the covalent linking of two different antibiotic moieties to produce a dimeric compound having improved activity (Ans. 3-4). The Examiner contends that "Truett I teaches a dimeric compound where one of the antibiotic moieties is ceftazidime . . .[,] a beta-lactam antibiotic that reads on the elected species," but concedes that "Truett I lacks the teaching of linking vancomycin with ceftazidime" (*id.* at 4).

To meet that limitation, the Examiner cites Truett II as disclosing the preparation of linked antibiotics "where a quinolone derivative is linked to a beta lactam, which, in turn, is linked to vancomycin. Thus Truett II . . . teaches linking a beta-lactam antibiotic to vancomycin in an antibiotic compound" (*id.*).

The Examiner cites Boeckh as disclosing that combination therapy using vancomycin and ceftazidime is well known in the art, and "is used 'to cover a broad spectrum of gram positive and gram negative bacteria'" (*id.* at 5 (quoting Boeckh 92)). The Examiner relies on Renoud-Grappin for its disclosure of covalently linking two different classes of antiviral molecules in order to combine the molecules' activities, and on Staroske for its

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[3] Examiner's Answer mailed April 18, 2007.

disclosure that covalently linked vancomycin dimers "exhibit improved antibacterial activity" (*id.* at 5-6).

Based on the teachings of the cited references, the Examiner contends that one of ordinary skill in the art "would have been motivated to covalently link vancomycin with ceftazidime to create a broad spectrum antibiotic compound to fight antibiotic resistant strains" (*id.* at 7).

Appellants contend that the Examiner failed to establish a prima facie case of obviousness based on the cited references (App. Br. 10-20; *see also* Reply Br.[4] 1-10). Appellants do not argue any of the claims separately (*see id.*). We select claim 41 as representative of the rejected claims. *See* 37 C.F.R. § 41.37(c)(1)(vii).

The issue with respect to this rejection, then, is whether the Examiner erred in concluding that one of ordinary skill would have considered claim 41 prima facie obvious in view of Truett I, Truett II, Boeckh, Renoud-Grappin, and Staroske.

FINDINGS OF FACT ("FF")

1. Claim 41 recites a compound having the basic formula:

L'-X'-L"

2. While claim 41 provides that the moieties L', X', and L" can have a number of different structures, Appellants elected to prosecute a compound in which L' is a β-lactam that encompasses ceftazidime, L" is vancomycin, and X' is a linkage through the vancosamine nitrogen atom of vancomycin (*see* Reply To Requirement for Restriction 3-4 (entered March 19, 2001);

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[4] Reply Brief filed June 13, 2007.

see also App. Br. 19 ("ceftazidime and vancomycin are the selected species")).

3. Truett I discloses that linking together two antibiotic moieties that function in different ways, "as for example inhibiting cell-wall synthesis or protein synthesis or DNA synthesis, can be of value. Two antibiotic moieties can also be linked in which one is known to attack Gram positive bacteria and another to attack Gram negative bacteria, and this new entity is of value" (Truett I, col. 1, ll. 25-30).

4. Truett I discloses that the two diverse antibiotic compounds can be covalently linked using "difunctional organic compounds such as diisocyanates, dianhydrides, diacidchlorides, diepoxides and carbodiimides," and that the antibiotic compounds amenable to this technique include "sulfonamides, penicillins and related, cephalosporins and related, quinolones, chloramphenicol, erythromycins, metronidazole, tetracyclines and aminoglycocides" (Truett I, col. 1, ll. 9-15).

5. Truett I lists ceftazidime among the cephalosporins and related molecules "of particular interest" in its methods (Truett I, col. 2, l. 49 through col. 3, l. 8). Truett I does not disclose linking ceftazidime to vancomycin, as recited in claim 41.

6. Truett II discloses:

> [A]n improved process for forming a single composition from two antibiotics, e.g., from Quinolone antibiotics and Beta-lactam antibiotics, as Penicillin and Cephalosporin types, and also with the addition of steps to add a third antibiotic component to the bi-component composition, the third (3^{rd}) antibiotic drawn from the group Vancomycin, Erythromycin, Azithromycin, an Aminoglycoside as Gentamycin, A Tetracycline, Clindamycin, and Chloramphenicol.

(Truett II, col. 1, ll. 13-21.) Thus, while Truett II discloses linking vancomycin to a beta-lactam, Truett II discloses that linkage only as part of a three-component compound that also contains a quinolone antibiotic.

7. Truett II discloses that "[t]he value of this composition of three antibiotic functional types is that . . . resistant strains will be very unlikely to develop due to the necessity of simultaneously overcoming three attacking agents" (Truett II, col. 1, ll. 28-31).

8. Boeckh "examined the pharmacokinetics and serum bactericidal activity of vancomycin-ceftazidime" in order to study "possible microbiological and pharmacokinetic interactions" of a therapeutic regimen using a combination of the two drugs (Boeckh 92).

9. Boeckh did not administer a combination of the two drugs covalently linked, as recited in claim 41. However, Boeckh discloses that "vancomycin is frequently used in serious infections in neutropenic cancer patients in combination with ceftazidime to cover a broad spectrum of gram-positive and gram-negative bacteria" (Boeckh 92).

10. Renoud-Grappin discloses the synthesis of heterodimer compounds comprised of a nucleoside reverse transcriptase inhibitor covalently linked to a different class of drug molecule, a non-nucleoside reverse transcriptase inhibitor, in an effort to combine the HIV-1 inhibitory properties of the two types of molecules (Renoud-Grappin 205). Renoud-Grappin discloses that antiviral drug combination therapies are "advocated for three main reasons: (i) additive or synergistic antiviral activity; (ii) diminished toxicity; and (iii) reduced risk of drug resistance development" (*id.* at 207).

11. Staroske discloses that, in view of "reports of vancomycin-resistant bacteria, there is a strong incentive for the development of more potential

antibiotics" (Staroske 4917). Staroske therefore synthesized "covalent dimers of vancomycin which are linked from C- to N-terminus (head-to-tail linkage) . . . . Such dimers have the potential to exploit additional cooperative interactions when binding to cell-wall precursors at a surface" (*id.* (abstract)). Staroske also discloses that certain derivatives of vancomycin "have potential for the synthesis of covalent vancomycin dimers linked *via* the vancosamine moiety" (*id.* at 4920).

PRINCIPLES OF LAW

> In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. "[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references."

In re Fritch, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (citations omitted, bracketed material in original). Thus, as the Supreme Court has pointed out, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

While holding that some rationale must be supplied for a conclusion of obviousness, the Supreme Court has nonetheless rejected a "rigid approach" to the obviousness question, and instead emphasized that "[t]hroughout this Court's engagement with the question of obviousness, our cases have set forth an expansive and flexible approach . . . ." *Id.* at 1739. The Court also rejected the use of "rigid and mandatory formulas" as being "incompatible with our precedents." *Id.* at 1741; *see also* 1742-43 ("Rigid

preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it.").

The Court thus reaffirmed "the conclusion that when a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." *Id.* at 1740 (quoting *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282 (1976)). The Court explained that a "patent for a combination which only unites old elements with no change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." *Id.* at 1739 (quoting *Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152 (1950)).

The Court reasoned that the analysis under 35 U.S.C. § 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id* at 1741. The Court further advised that "[a] person of ordinary skill is . . . a person of ordinary creativity, not an automaton." *Id.* at 1742.

Regarding hindsight reasoning, the Court stated that "[a] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. Rigid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it." *Id.* at 1742-43 (citations omitted).

ANALYSIS

We agree with the Examiner that the cited references would have rendered claim 41 prima facie obvious to a person of ordinary skill in the art. Truett I would have advised one of ordinary skill in the art that it was desirable to make dimeric compounds composed of two different antibiotic moieties having different activities (*see* FF 3, 4), and that ceftazidime was "of particular interest" for use in such dimeric compounds (Truett I, col. 2, l. 49 through col. 3, l. 8 (FF 5)).

While Truett I differs from claim 41 in not linking ceftazidime to vancomycin, Truett I nonetheless would have advised one of ordinary skill in the art of the desirability of linking "[t]wo antibiotic moieties . . . in which one is known to attack Gram positive bacteria and another to attack Gram negative bacteria" (Truett I, col. 1, ll. 27-30 (FF 3)). One of ordinary skill would have been further advised by Boeckh that the combination of vancomycin and ceftazidime "cover[s] a broad spectrum of gram-positive and gram-negative bacteria" (Boeckh 92 (FF 9)).

Thus, we agree with the Examiner that one of ordinary skill in the art, being a person of ordinary creativity and common sense, *see KSR*, 127 S. Ct. at 1742-43, recognizing from Boeckh that the combination of vancomycin and ceftazidime treated a broad spectrum of both gram positive and gram negative bacterial infections, and further recognizing from Truett I that it was desirable to covalently link two antibiotic moieties having activity against gram positive and gram negative bacteria, would have been prompted to covalently link vancomycin to ceftazidime, as recited in claim 41. Given the further teachings in Truett II and Staroske of vancomycin's capacity for covalent linkage in multimeric antibiotic compounds (*see* FF 6,

7, and 11), and the disclosures in Truett II and Renoud-Grappin of the advantages of combination therapies using covalently linked antibiotic compounds, including the reduced risk of drug resistance (*see* FF 7, 10), we agree with the Examiner that one of ordinary skill in the art would have considered claim 41 prima facie obvious in view of the cited references.

Appellants argue that one of ordinary skill in the art would not have been motivated to combine the references in the manner advanced by the Examiner because the ordinary artisan would have expected that so doing would render the prior art compounds unsuitable for their intended functions (App. Br. 11-14; *see also* Reply Br. 3-6). Specifically, Appellants urge that Truett II only discloses the suitability of linking vancomycin to a beta-lactam when a quinolone is also linked to the beta-lactam, and that therefore, "there is no evidence that linking a beta-lactam antibiotic with vancomycin will work for its intended purpose" (App. Br. 14). Appellants similarly argue that Truett II teaches away from covalently linking vancomycin to only ceftazidime because Truett II only discloses that it is desirable to link vancomycin to a beta-lactam when a quinolone is also linked to the beta-lactam (*id.* at 14-15; *see also* Reply Br. 6-7).

We are not persuaded by these arguments. We note that the Supreme Court has stated that claims are likely to be unobvious "when the prior art teaches away" from their practice. *KSR*, 127 S. Ct. at 1740. The Court has therefore held claims to be unobvious where the prior art warned of risks involved in using the claimed elements. *Id.* (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1966)). Similarly, as stated by our reviewing court, "[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out

in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Kahn*, 441 F. 3d 977, 990 (Fed. Cir. 2006) (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994)).

In the instant case, while Truett II may only disclose linking vancomycin to a beta-lactam when a quinolone is also linked to the beta-lactam, we do not see, and Appellants do not point to, any specific disclosure in Truett II stating that it would be undesirable, or unsuitable, to covalently link vancomycin to a beta-lactam in the absence of the quinolone. We therefore do not agree with Appellants that Truett II teaches away from combining vancomycin and ceftazidime in the manner recited in claim 41.

Moreover, it is well settled that "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole." *In re Merck & Co., Inc.*, 800 F.2d 1091, 1097, (Fed. Cir. 1986).

Thus, in the instant case, the teachings of Truett II may not be viewed alone, but instead must be viewed alongside the teachings of the other references. As discussed above, Truett I discloses the suitability, and desirability, of making an antibiotic compound composed of only two antibiotic moieties, and further discloses that it was particularly desirable to combine two antibiotics having activity against gram positive and gram negative bacteria (FF 3).

Given the disclosures of Truett II and Staroske that vancomycin does not lose activity when covalently linked to other moieties (FF 6, 7, 11), we agree with the Examiner that one of ordinary skill would have reasonably

inferred that vancomycin would be useful as one of the two antibiotic moieties in the compounds of Truett I, particularly given the wide variety of antibiotic moieties disclosed by Truett I as being useful in its compounds (FF 4). Given Truett I's teaching of the desirability of covalently linking antibiotics active against gram positive and gram negative bacteria (FF 3), combined with Boeckh's disclosure that the ceftazidime-vancomycin combination was a known therapy regimen against infections by gram positive and gram negative bacteria (FF 9), we also agree with the Examiner that one of ordinary skill in the art would have been prompted to covalently link ceftazidime and vancomycin in the manner recited in claim 41.

Appellants argue that the Examiner has not provided a basis for selecting ceftazidime from the 69 compounds named in Truett I (App. Br. 15-16). Rather, Appellants argue, the Examiner "only highlights the use of hindsight reasoning to select ceftazidime" from among the compounds disclosed by Truett I (*id.* at 16).

Appellants further argue that it is unreasonable "to select one compound (ceftazidime) out of the 69 compounds disclosed in the reference given that the reference provides absolutely no guidance to select one compound over another. In fact, considering Truett I as a whole, the reference actually supports Appellants' position that ceftazidime is no more important than any other compound of Truett I" (*id.* at 17; *see also* Reply Br. 7-8). Appellants further urge that one of ordinary skill would not have been motivated to covalently link vancomycin and ceftazidime in view of Boeckh's disclosure of the administration of ceftazidime and vancomycin as separate compounds "within a mixture without any apparent disadvantages, including any inconveniences" (App. Br. 18; *see also* Reply Br. 8-9).

We are not persuaded by these arguments. While ceftazidime may be only one of 69 compounds disclosed by Truett I as being useful in its compounds, Truett I explicitly states that it is a cephalosporin that is "of particular interest" in its methods (Truett I, col. 2, l. 49 through col. 3, l. 8 (FF 5)).

Moreover, in *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989), our reviewing court held a species claim obvious over a reference disclosing over 1200 possible combinations of two ingredient types useful in diuretic compositions. Neither of the claimed ingredients was listed by the reference as being preferred. *Id.* The court nonetheless held the claims to be obvious in view of the reference's explicit teaching that any one of the claimed compositions would produce a diuretic composition having desirable properties. *Id.*

Thus, we do not agree with Appellants that selecting a compound disclosed as being of particular interest would be considered unobvious merely because it is contained within a group of 69 possibilities. Further, given the other references' disclosures that that compound, ceftazidime, is suitably combined with vancomycin to treat a broad spectrum of gram positive and gram negative bacterial infections (FF 9), and that it is desirable to covalently link two compounds capable of treating gram positive and gram negative bacterial infections (FF 3), we agree with the Examiner that one of ordinary skill in the art would have been prompted to combine ceftazidime and vancomycin in the manner recited in claim 41.

Appellants argue that a showing of obviousness requires a specific suggestion or motivation to practice the claimed subject matter, and that "[w]hile there may be a general desire in the art to create broad spectrum

antibiotics, this general desire alone is not enough to provide motivation to link the two specific antibiotics of the claimed invention (ceftazidime and vancomycin are the selected species)" (App. Br. 19). Following the Examiner's logic, Appellants argue, "the desire and need for broad spectrum antibiotics would render virtually any new broad spectrum antibiotic obvious. This simply cannot be the standard" (*id.*).

We are not persuaded by these arguments. For the reasons discussed above, we agree with the Examiner that the cited references would have prompted one of ordinary skill in the art to covalently link ceftazidime to vancomycin in the manner recited in claim 41.

Thus, because we agree with the Examiner that claim 41 would have been prima facie obvious to a person of ordinary skill in the art in view of Truett I, Truett II, Boeckh, Renoud-Grappin, and Staroske, we affirm the Examiner's rejection of claim 41. Because Appellants did not present separate arguments with respect to claims 43, 49-51, and 53-55, those claims fall with claim 41. 37 C.F.R. § 41.37(c)(1)(vii).

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

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